

SPL Process Meeting Meeting Minutes May 22, 2013

Chair of today's meeting: Pat Cowall-Hanover

Teleconference information:

USA Toll-Free 866-213-2145

USA Paid/International: 609-454-9913

Access code: 273 8216

Teleconference information: How to mute/unmute

#6: Mute

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Meeting notes:

Coming attractions

1. Updates from SPL Lead and Tech team meetings

- a. Reminder to Manufacturers to submit Final SPLs in a timely manner—ie per instructions in FDA Approval Letter
 - FDA has been encouraging the use of SPL and Daily Med for several years. FDA reviewers are now looking at Daily Med and noticing that some files aren't being updated in a timeline manner. Lonnie gets 1-2 emails per week asking why files aren't there – not within the 14 days as stated in the approval letters, but even as long as 6 months after approval.
 - Lonnie asked us to communicate this out to the Teams. This could result in a complaint from your FDA reviewer.
 - Impact: If the SPL is not in Daily Med, then the information won't get to any downstream users – 3rd party payers, data out to patients, etc They are going to the fastest way to get to the data.
 - Problem: Real issue is when the file is on a company's website and is not in Daily Med. ie the company is choosing not to put the file on Daily Med.
 - DailyMed now has over 50,000 SPLs. And this doesn't even include API, in process, OTC, etc.
 - What happens if the company is not planning to market this for a while?
 - Put in a future marketing date.
 - As you are getting close to approval, communicate with FDA that you aren't planning to market it for a while, and ask FDA to note this in their files and adjust the text in the approval letter such that they don't require drug listing in 14 days.
 - The only way to get a file to Daily Med is through drug listing.

- b. Coding of Revision Date in SPL-PLR Highlights Area – optional coding to add approval/implementation date of USPI
- Question has come up over the years as to how to represent the revision date.
 - 2006 the revision date is the approval date for the highlights. FDA was adding the date to the SPL system. These dates were different to the approval date.
 - 2009: FDA said sponsors could use whatever date they chose as the version date on the SPL file
 - The SPL version date populates the highlights date and the revision date to the SPL.
 - This is no problem when the USPI changes.
 - This presents an issue when other sections of the SPL change – ie not the USPI, but the cartons/labels, DPL date, etc.
 - Companies use different processes for updating the SPL revision date-
 - a. some always use the date on the USPI.
 - b. Some use the date of SPL revision. Thus the date in the SPL highlights represents the SPL revision date, and not the date of USPI approval.
 - FDA is adding an optional data element – revision date that will appear in the highlights ...that is different from the SPL revision date.
 - This is the optional coding because FDA can't change the stylesheet to this across all SPL, because there are 50,000 SPL files on Daily Med that do not have this data element.
 - If this data element exists, the highlights will show this date. If the data element doesn't exist, it will display the spl revision date.
 - The implementation guide will also updated.
 - Where will this optional data element be placed in the code? Within the DLDE data for each product. This could be different for each product – if the USPI didn't change. See coding below.
 - Look at the PLR guidance document to determine what CDER is expecting to be in the date at the bottom of the highlights section.

Labeling for Human Prescription Drug and Biological Products – Implementing the PLR Content and Format Requirements

Website:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm075082.pdf>

- **Discussions are still underway as to how to code this.**
- **Implementation date: FDA has not updated the stylesheet yet. We are expecting an announcement.**

c. SPL NDC Labeler Code Request - CVM

- FDA CVM division wants a different document type for their labeler codes. A new SPL document type has been established and is on the SPL resource pages.

LOINC code="72871-7" displayName="NDC LABELER CODE REQUEST - ANIMAL DRUG"

- Additional data elements will also be added to the labeler request form for animal drugs. Following receipt of the initial request, FDA has to send questions out in an email to get additional data. So these additional data elements will eliminate the need for the extra email.
- Existing labeler request for human pharma doesn't apply to CVM companies, and CVM didn't want their companies to have to struggle with these questions.
- This will take a couple of months to finalize. This will allow vendors time to update their tool.

d. Use of Ingredient classCode="ADJV" (Adjuvant) for CBER Vaccine Products

- Probably only for vaccines... Adjuvant are not active ingredient or inactive ingredients. It is something else. So CBER/CDER will like to see adjuvant included.
- Per Mary Beth, an adjuvant increases the patient's immune response to the vaccine so the vaccine works better without having to add more antigen (more antigen can cause more adverse reactions).
- You need to tell your vendors that ingredients are adjuvant. The compounds are probably also in the SPL as inactive ingredients.
- Per Lonnie, he said that it will soon be apparent why this is important.
- If you have the coding in today, it will go through and/or it won't be a problem.

2. Upcoming SPL requirements for Medical Devices? I believe one of the requirements is to publish device information to an FDA maintained Global Unique Identifier Database (GUDID). (Robb Wirt) Myron Finseth led the discussion on this topic.

- We are currently waiting for a proposed rule – UDI - expected in June.
- They will start out with high risk (Type 3) devices. Likely to start this summer.
- How to get data into the UDI database? Unknown, possibly a web portal, possibly using an SPL submission. Not well known outside of CDRH.
- Once the final rule is posted, we will learn more. Possibly in June.
- There was a workshop in April about device labeling, they discussed home use devices. Learned that industry needs a standardized structure for Table of Contents for Device IFUs. Lots of arguments about a central repository (pros and cons). Device industry has a steep learning code. They don't know advantages of using structured content.

3. Discuss FDA's revised requirements for drug listing starting in October, particularly around what additional information will now be required to be listed for active and excipient ingredient suppliers. (Beth Thompson)

- Change in October related to Establishment Registration. As of Oct, 2012, all establishments need to submit their annual Establishment Registration (DER) between

Oct 1 and Dec 31 for the following year. Updates should be made throughout the year to maintain their DER.

- i. These would not fulfill the annual registration requirement unless the update is submitted between Oct 1 and Dec 31.
- Excipient: This is a new FDASIA requirement. FDA has not yet published instructions on how to implement this.
 - Charisse Kasser (FDA CVM) provided comment. She sits on the working group. They haven't figured out what they want to do yet.

Current process questions:

4. Question from SPL OTC sub-team member: If a branded drug has a labeling change, what section in the CFR covers updating the generic? Would the generic drug just be updated to match, and then reported via the annual report, or would a supplement be required? (Marcia Howard)

FDA Response:

Information regarding when and how Abbreviated New Drug Application (ANDA) sponsors should submit labeling supplements following labeling revisions to their reference listed drugs (RLDs) may be found in the Guidance for Industry "Revising ANDA Labeling Following Revision of the RLD Labeling". The Guidance states that when a New Drug Application (NDA) serves as a reference listed drug (RLD) for an Abbreviated New Drug Application (ANDA), approved changes in the RLD labeling generally necessitate changes in the labeling of one or more ANDAs using the RLD. Under the Federal Food, Drug, and Cosmetic Act [21 U.S.C.] and Agency regulations, an ANDA product must have the same labeling as the RLD. You may review this Guidance online at:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072891.pdf>.

Section 505(j)(2)(A)(v) of the Act [21 U.S.C. 355] states that an abbreviated application for a new drug must contain information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug, except for changes required because of differences approved under a petition, or because the new drug and the listed drug are produced or distributed by different manufacturers. Similar statements are also found in the regulations at 21 CFR 314.94(a)(8)(iv).

21 CFR 314.94(a)(8)(iv) states:

"Comparison of approved and proposed labeling.

A side-by-side comparison of the applicant's proposed labeling including, if applicable, any Medication Guide required under part 208 of this chapter with the approved labeling for the reference listed drug with all differences annotated and explained. Labeling (including the container label, package insert, and, if applicable, Medication Guide) proposed for the drug product must be the same as the labeling approved for the reference listed drug, except for changes required because of differences approved under a petition filed under 314.93 or because the drug product and the reference listed drug are produced or distributed by different manufacturers. Such differences between the applicant's proposed labeling and labeling approved for the reference listed drug may include differences in expiration date, formulation, bioavailability, or pharmacokinetics, labeling revisions made to comply with current FDA labeling guidelines or other

guidance, or omission of an indication or other aspect of labeling protected by patent or accorded exclusivity under section 505(j)(5)(F) of the act."

You may review 505(j)(2)(A)(v) of the Act online at: <http://www.gpo.gov/fdsys/pkg/USCODE-2010-title21/pdf/USCODE-2010-title21-chap9-subchapV-partA-sec355.pdf> (page 166 - page 9 of the 34 page PDF document) and

21 CFR 314.94 online at: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm>.

How do you submit it? Annual report or Supplement?

- FDA didn't give us a specific timing. You need to review the citations.
- Response from a teammember: They submit as a CBE0, per instructions in one of the citations.

5. After speaking to our labeling colleagues regarding the assignment of NDC numbers on blister packs, we were just wondering if anyone has experience with assigning a separate NDC number on their blister packs that is different from the carton it goes into? This way, that blister can be reused in different carton sizes (i.e. an 8ct blister having a unique NDC number can be used in the 16ct pkg, 24ct pkg, 32ct pkg, etc. with all having different outer NDC numbers on their cartons). Therefore, when drug listing the package, you would specify a different NDC number for the inner (i.e. the blister) and a different NDC number on the outer (i.e. the carton). Is this common? We just recently encountered packaging that we are looking to do this. Any pros/cons instead of having the blister contain the same NDC as the outer package carton? (Mary Beth Kline)

Question:

- Should we assign separate NDC codes for the blister?
 - Yes, You shouldn't put the same NDC package code on the blister versus on the carton.
 - BMS: blister card of 8 versus carton of 16. They both use same product code but different package codes.
 - This is valid for CDER products.
 - Per Howard: There is an issue with Daily Med stylesheet. It appears wrong. The FDA stylesheet displays it correctly.
6. If a product is not currently manufactured or distributed (ANDA is active) and a safety/non-safety labeling submission is made to be in line with the RLD, should the most updated SPL be posted on dailymed? (Ranjith Abraham-Ranbaxy)
- If the product is still in the marketplace, they still need update drug listing.
 - What is considered the market end date in SPL?
 - This is defined as the date of expiry of the last lot of material.

7. Is drug-listing (sending the SPL file through ESG) the only way to update dailymed? Does FDA update DailyMed with the SPL that is a part of most of the labeling submissions (eg., RLD Updates)? (Ranjith Abraham- Ranbaxy)

Yes. The only way to get SPL on Daily Med is by drug listing it.

Meeting ended here!

Save this topic for the next meeting.

8. I recalled that the group had discussed the marketing date versus approval date in the past. Where can I find this topic in the Wiki? Also, for DailyMed postings, if there is a minor change in labeling and implementation into packaging will be at the next packaging run, it is my understanding that the marketing start date can be set in the future, i.e months ahead. (Gil Granados)
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